

Entrusted to operate the C.W. Bill Young Cell Transplantation Program, including Be The Match Registry®

October 31, 2011

CDR Sheri Parker Office of Naval Research (ONR 342) 875 N. Randolph St. Arlington, VA 22203-1995

Subject:

Quarterly Performance/Technical Report of the National Marrow Donor

Program<sup>®</sup>

Reference:

Grant Award #N00014-11-1-0339 between the Office of Naval Research and the

National Marrow Donor Program

Dear Cdr. Parker:

Enclosed is subject document which provides the performance activity for each statement of work task item of the above reference for the period of July 1, 2011 to September 30, 2011.

Should you have any questions as to the scientific content of the tasks and the performance activity of this progress report, you may contact our Chief Medical Officer – Dennis L Confer, MD directly at 612-362-3425.

With this submittal of the quarterly progress report, the National Marrow Donor Program has satisfied the reporting requirements of the above reference for quarterly documentation. Other such quarterly documentation has been previously submitted under separate cover.

Please direct any questions pertaining to the cooperative agreement to my attention at 612-362-3403 or at <a href="mailto:cabler@nmdp.org">cabler@nmdp.org</a>.

Sincerely,

Carla Abler-Erickson, MA

Sr. Contracts Representative

Enclosure: Quarterly Report with SF298

Cula Abler Encloser

C: D. Ivery – ACO (ONR-Chicago)

Dr. Robert J. Hartzman, CAPT, MC, USN (Ret)

Jennifer Ng, PhD - C.W. Bill Young Marrow Donor Recruitment and Research Program

J. Rike - DTIC (Ste 0944)

NRL (Code 5227)

Dennis Confer, MD, Chief Medical Officer, NMDP

Stephen Spellman

# REPORT DOCUMENTATION PAGE

Form Approved OMB No. 0704-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Washington Headquarters Service, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188) Washington, DC 20503.

1215 Jefferson Davis Highway, Suite 1204, Arlingto Paperwork Reduction Project (0704-0188) Washing	n, VA 22202-43	302, and to the Office of Ma		mation operation	one and reports,
PLEASE DO NOT RETURN YOUR FO			SS.		
. REPORT DATE (DD-MM-YYYY) 1-10-2011 2. REPORT TYPE Quarterly			3. DATES COVERED (From - To) Jul - Sep 2011		
4. TITLE AND SUBTITLE  Development of Medical Technology for Contingency Response to			5a. CONT	TRACT NUMBER	
Marrow Toxic Agents - Quarter	ly Perforr	mance/Technical			
July 01, 2011 to September 30	, 2011 Pe	eriod 3		<b>5b. GRANT NUMBER</b> N00014-11-1-0339	
				5c. PROON	GRAM ELEMENT NUMBER
6. AUTHOR(S) Spellman, Stephen				5d. PRO	JECT NUMBER
					K NUMBER 1, 2, 3, 4
				5f. WOR	K UNIT NUMBER
				14/74	
7. PERFORMING ORGANIZATION NA National Marrow Donor Program 3001 Broadway St., N.E., Ste. & Minneapolis, MN 55413	m	D ADDRESS(ES)			8. PERFORMING ORGANIZATION REPORT NUMBER N/A
Willingapolio, Will 00410					
9. SPONSORING/MONITORING AGE Office of Naval Research	NCY NAME	E(S) AND ADDRESS	S(ES)		10. SPONSOR/MONITOR'S ACRONYM(S) ONR
875 N. Randolph St. Arlington, VA 22203					11. SPONSORING/MONITORING AGENCY REPORT NUMBER N/A
12. DISTRIBUTION AVAILABILITY ST Approved for public release; dis					
13. SUPPLEMENTARY NOTES N/A					
14. ABSTRACT					
1. Contingency Prepardnes					uild awareness of the Transplant Center cal importance of establishing a nationwide
2. Rapid Identification of Mapatient access are key to prepared			e operational effi	ciencies th	at accelerate the search process and increase
3. Immunogenetic Studies:	Increase u	inderstanding of th	ne immunologic	factors imp	portant in HSC transplantation.
	antation:	Create a platform	that facilitates r	nulticenter	collaboration and data management.
15. SUBJECT TERMS Research in HLA Typing, Hema	atopoietic	: Stem Cell Trans	splantation and	Clinical S	Studies to Improve Outcomes
16. SECURITY CLASSIFICATION OF	:	17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES		DF RESPONSIBLE PERSON  Confer, MD – Chief Medical Office
a. REPORT b. ABSTRACT c. TH	IS PAGE	Same as Report	19	19b. TELEPO	ONE NUMBER (Include area code)

#### NATIONAL MARROW DONOR PROGRAM®

Creating Connections. Saving Lives.™

# Grant Award N00014-11-1-0339

# DEVELOPMENT OF MEDICAL TECHNOLOGY FOR CONTINGENCY RESPONSE TO MARROW TOXIC AGENTS QUARTERLY PERFORMANCE / TECHNICAL REPORT FOR JULY 01, 2011 to SEPTEMBER 30, 2011 PERIOD 3

Office of Naval Research

And

The National Marrow Donor Program 3001 Broadway Street N.E.
Minneapolis, MN 55413
1-800-526-7809

#### QUARTER PROGRESS REPORT

	TABLE OF CONTENTS		
TASK	DESCRIPTION	STATUS	PAGE
IIA	Contingency Preparedness		
IIA.1	Objective 1 – Care Plans by Transplant Physicians		
	Task 1 – Secure Interest of Transplant Physicians	Open	4
	Task 2 – GCSF in Radiation Exposure	Open	4
	Task 3 – Patient Assessment Guidelines	Open	4
	Task 4 – National Data Collection and Management Model	Closed	4
IIA.2	Objective 2 – Coordination of Care of Casualties		
	Task 1 – Contingency Response Network	Open	4
	Task 2 – Standard Operating Procedures	No Activity	6
IIA.3	Objective 3 – Information Technology Infrastructure		
	Task 1 – Disaster Recovery	No Activity	6
	Task 2 – Critical Facility and Staff Related Functions	Open	6
II.B	Rapid Identification of Matched Donors	•	
II.B.1	Objective 1 – Resolution of Speeds Donor Selection		
	Task 1 – Increase Registry Diversity	Open	7
	Task 2 – Evaluate HLA-DRB1 High Resolution Typing	Closed	7
	Task 3 – Evaluate HLA-C Typing of Donors	Closed	7
	Task 4 – Evaluate Buccal Swabs	No Activity	7
	Task 5 – Enhancing HLA Data for Selected Donors	Closed	7
	Task 6 – Maintain a Quality Control Program	Open	7
IIB.2	Objective 2 – Improve HLA Quality & Resolution		
	Task 1 – Collection of Primary Data	No Activity	8
	Task 2 – Validation of Logic of Primary Data	Closed	8
	Task 3 – Reinterpretation of Primary Data	Closed	8
	Task 4 – Genotype Lists & Matching Algorithm	Open	8
IIB.3	Objective 3 – Algorithm to Predict Best Donor		
	Task 1 – Incorporate Frequencies into Matching Algorithm	Open	8
	Task 2 – Enhancement of EM Algorithm	Open	9
	Task 3 – Optimal Registry Size Analysis	Open	9
	Task 4 – Target Underrepresented Phenotypes	Open	9

#### QUARTER PROGRESS REPORT

	Acronym List		17
	Task 3 – Expand Immunobiology Research	Open	16
	Task 2 – Research with NMDP Donors	Closed	16
	Task 1 – Observational Research, Clinical Trials and NIH Transplant Center	Open	12
IID.1	Objective 1 – Clinical Research Improves Outcomes		
IID	Clinical Research in Transplantation		
	Task 3 – CIBMTR Integration	Closed	12
	Task 2 – Related Pairs Research Repository	Closed	12
	Task 1 – Analysis of Non-HLA Loci	Open	11
IIC.2	Objective 2 – Role of Other Loci and GVHD	•	
	Task 1 – Donor Recipient Pair Project	Open	11
IIC.1	Objective 1 – Influence of HLA Mismatches		
IIC.	Immunogenetic Studies		-
	Task 4 – Expand Capabilities of Collection and Apheresis Centers	Closed	10
	Task 3 – Benchmarking Analysis	Closed	10
	Task 2 – Central Contingency Management	Open	10
	Task 1 – Expand Network Communications	Closed	10
IIB.4	Objective 4 – Reduction of Donor Matching Time	Closed	10
	Task 9 – Global Haplotype/Benchmark	Closed	10
	Task 8 – Haplotype Matching	Closed	10
	Task 7 – Population Genetics	Closed	10
	Task 6 – Utilize Search Strategy Advisors to Improve Algorithm	Closed	10
	Task 5 – Bioinformatics Web Site	Closed	10

<b>IIA. Contingency Preparedness</b> – <b>Objective 1:</b> Recovery of casualties with significant myelosuppression following radiation or chemical exposure is optimal when care plans are designed and implemented by transplant physicians				
IIA.1 Task 1: Secure				
Interest of Transplant Physicians	<ul> <li>Continued planning of the Advanced Medical Radiation Response training to be held on October 17-18 at the Radiation Emergency Assistance Center and Training Site in Oakridge, TN</li> </ul>			
IIA.1 Task 2: GCSF in	Period 3 Activity:			
Radiation Exposure	<ul> <li>Conference planner worked on the preparations for the RITN State of the Science Workshop: Radiation Exposure, Medical Countermeasures and Treatment</li> </ul>			
IIA.1 Task 3: Patient	Period 3 Activity:			
Assessment Guidelines and System Enhancements	<ul> <li>Planning was conducted for the October State of the Science Workshop: Radiation Exposure, Medical Countermeasures and Treatment</li> </ul>			
IIA 1 Task 4: National I	Data Collection Model – This task is closed.			
<b>IIA.</b> Contingency Preparate be essential in a contingency	<b>aredness</b> – <b>Objective 2:</b> Coordination of the care of casualties who will require hematopoietic support will ncy situation.			
IIA.2 Task 1:	Period 3 Activity:			
Contingency Response Network	<ul> <li>Conducted site assessments of five (5) RITN transplant centers; assessments reviewed critical areas necessary for responding to a mass casualty incident with marrow toxic injuries</li> </ul>			
	o These areas are: victim processing, outpatient treatment of victims, inpatient treatment of victims, coordination with region, state or federal agencies; documentation review			
	Currently RITN consisted of: 47 – transplant centers, 7 - donor centers, and 7 - cord blood banks			
	<ul> <li>23 centers were identified as potential new RITN center candidates</li> </ul>			
	<ul> <li>An invitation to join RITN was extended to each based on their participation as an NMDP transplant center and being part of the National Disaster Medical System (this ensures reimbursement for care provided)</li> </ul>			

- o Eight (8) of these centers have accepted the invitation and formally joined RITN
- o Additionally, one (1) center that previously left the network rejoined
- o Unfortunately, one (1) center declined
- o Ten (10) centers have not responded
- 3% (qty: 2) of RITN centers have completed all of the required annual tasks, deadline is December 31, 2011
  - o Previous year's data: FY10-94%, FY09-98%, FY08-96%, FY07-96%, FY06-92%
- RITN Medical Advisor activity; Dr. Weinstock prepared for participation in the following activities supporting the Radiation Injury Treatment Network:
  - He will be a featured speaker on the response to the Fukushima Daiichi nuclear power plant incident by the HSCT community at the RITN State of the Science Meeting in Chicago, IL on October 11, 2011
  - He co-Chaired the Planning Committee for the RITN State of the Science Meeting in Chicago, IL on October 11, 2011
  - He will be the moderator of the RITN Executive Committee Roundtable Discussion in Chicago, IL on October 11, 2011
  - o He co-authored:
    - The manuscript, "Radiation Injury Treatment Network (RITN): Healthcare Professionals Preparing for a Mass Casualty Radiological or Nuclear Incident" in the International Journal of Radiation Biology; August 2011
    - The manuscript, "First Global Consensus for Evidence-Based Management of the Hematopoietic Syndrome Resulting From Exposure to Ionizing Radiation" in Disaster Medicine and Public Health Preparedness; October 2011
    - The manuscript, "Literature Review and Global Consensus on Management of Acute Radiation Syndrome Affecting Non-Hematopoietic Organ Systems" in Disaster Medicine

	and Public Health Preparedness; October 2011		
	<ul> <li>A manuscript in preparation for <u>Biosecurity and Bioterrorism</u>: <u>Biodefense Strategy</u>,</li> <li><u>Practice</u>, and <u>Science</u></li> </ul>		
	<ul> <li>A manuscript in preparation for <u>Leukemia</u> on response to the Fukushima Daiichi nuclear power plant incident</li> </ul>		
	<ul> <li>A manuscript in preparation for <u>Lancet</u> on response to radiation incidents</li> </ul>		
	<ul> <li>He is assisting with the update of the RITN-sponsored online NMDP Radiation Basic Training Course</li> </ul>		
	<ul> <li>He consulted on updates to the Radiation Emergency Medical Management website (REMM)</li> </ul>		
	<ul> <li>He helped plan a session describing interactions between RITN and the National Disaster Medical System for the upcoming 2012 Integrated Summit in Memphis, TN</li> </ul>		
	Conducted the monthly RITN Center conference call to review task completion status and allow a venue for centers to talk to peers		
IIA.2 Task 2: Sibling	Period 3 Activity:		
Typing Standard Operating Procedures	No activity during this reporting period.		
	<b>aredness</b> – <b>Objective 3:</b> NMDP's critical information technology infrastructure must remain operational tions that directly affect the Coordinating Center.		
IIA.3 Task 1:	Period 3 Activity:		
I.S. Disaster Recovery	No activity during this reporting period		
IIA.3 Task 2:	Period 3 Activity:		
Critical Facility and Staff Related Functions	<ul> <li>Conducted an operations continuity exercise (BCPeX 2011) which permitted 11 NMDP departments to remotely conduct operations and successfully test 85% of critical tasks</li> </ul>		
	<ul> <li>Critical Task List Review Committee reviewed and approved program updates by deleting obsolete tasks and approving new critical tasks</li> </ul>		

# Development of Medical Technology for Contingency Response to Marrow Toxic Agents April 01, 2011 through June 31, 2011

• Initiated Operations capacity review to determine impact of case management staffing on current service level agreements

**IIB. Rapid Identification of Matched Donors – Objective 1:** Increasing the resolution and quality of the HLA testing of volunteers on the registry will speed donor selection.

#### IIB.1 Task 1:

# Increase Registry Diversity

#### **Period 3 Activity:**

- During the quarter, NMDP staff continued to manage and fine-tune the recently implemented strategy to enhance donor recruitment typing through optimal use of NMDP contracted labs. The strategy preferentially targets younger and minority donors and directs their samples to laboratories providing higher resolution typing as well as HLA-C.
- In addition, the ongoing project of reviewing rare alleles reported on donors in the Be The Match Registry continued. 95 donors with rare alleles were identified and retyped. To date, 1150 samples have been sent to a contract laboratory for high resolution typing at A, B, C, or DRB1. In total, 903 (60%) donor typings have changed from the previously reported rare allele and 605 donor typings have been confirmed to carry the reported rare allele.

**IIB.1 Task 2:** Evaluate HLA-DRB1 High Res typing – This task is closed.

**IIB.1 Task 3:** Evaluate HLA-C Typing of Donors – This task is closed

# **IIB.1 Task 4:** Evaluate Buccal Swabs

#### **Period 3 Activity:**

• No activity this reporting period.

**IIB 1 Task 5:** Enhancing HLA Data for Selected Donors – This task is closed.

#### **IIB** 1 Task 6:

### Maintain a Quality Control Program

#### **Period 3 Activity:**

During this quarter, 83 samples from the Research Repository were selected for incorporation into the NMDP QC program and were sent for cell culture/initiation/expansion, 70 in July and 13 in August 2011. Six of the 83 samples had negative growth and 1 is questionable. Twenty-seven additional samples will be sent for cell culture/initiation/expansion in October 2011. Ninety-nine of the 110 will be sent for HR-HLA A, C, B, DRB1, DRB3/4/5, DQB1, DPB1 confirmatory typing to ensure accuracy of typings entered into the QC database.

	These 104 samples ensure that the NMDP QC inventory has complete coverage of all but 5 CWD common		
	US alleles, and expand alleles that were depleted to an n of 1.		
	tion of Matched Donors – Objective 2: Primary DNA typing data can be used within the registry to resolution of volunteer donor HLA assignments.		
IIB 2 Task 1:	Period 3 Activity:		
Collection of Primary Data	No activity during this reporting period.		
IIB 2 Task 2: Validation	on of Logic of Primary Data – This task is closed.		
IIB 2 Task 3: Reinterpr	retation of Primary Data – This task is closed.		
_	<ul> <li>Period 3 Activity:</li> <li>Personnel: Hired Data/Business Analyst (Bob Milius)</li> <li>HL7: NMDP became member of HL7, and began evaluating HL7 messaging type (V2 &amp; V3), methodology, and development tools</li> <li>caBIG Life Sciences Domain Analysis Model: initiated contact with the LS-DAM group; began work to include HLA in LS-DAM (either map to current model or expand to include new concepts as needed)</li> <li>ion of Matched Donors – Objective 3: Registry data on HLA allele and haplotype frequencies and on the can be used to design computer algorithms to predict the best matched donor.</li> </ul>		
IIB.3 Task 1: Phase I of EM Haplotype Logic	<ul> <li>Period 3 Activity:         <ul> <li>The following improvements to the HapLogic algorithm were completed during this reporting period as follows:</li></ul></li></ul>		

	to accommodate new information such as x/8 and x/10 match percentages.				
	<ul> <li>Revised and enhanced the HapLogic-tools user interface, which was specifically developed for users of HapLogic 3.</li> </ul>				
	Completed multiple rounds of algorithm validation using various sets of preliminary 6-locus haplotype frequency data				
IIB 3 Task 2:	Period 3 Activity:				
Enhancement of EM Algorithm	<ul> <li>Calculated 6-locus A~C~B~DRB3/4/5~DRB1~DQB1 haplotype frequencies on 21 detailed race populations and 5 rollup race populations using Blocks/Imputation EM approach on the entire DNA-typed registry.</li> </ul>				
	<ul> <li>Tested 6-locus haplotype frequencies in a development version of the HapLogic III matching algorithm and found significant improvements in predictions of allele matching compared to the production Maiers 2007 haplotype frequency dataset.</li> </ul>				
IIB 3 Task 3: Optimal	Period 3 Activity:				
Registry Size Analysis	Revised and submitted Math Model manuscript to the journal Tissue Antigens.				
	<ul> <li>Developed draft of Registry Models Physician-Oriented manuscript in collaboration with Dr. Mary Eapen of CIBMTR.</li> </ul>				
IIB 3 Task 4:	Period 3 Activity:				
Target Under- Represented Phenotypes	Loaded the new IMP_RES database with imputed and normalized HLA information, demographic data, and a calculated diversity score based on genotype-predicted-likelihood.				
	<ul> <li>Built 40,000 country-specific BMDW maps utilizing our automated process.</li> </ul>				
	Completed posters accepted at the ASHI and ASHG annual conferences for sharing importance and usefulness of Global BMDW maps.				
	<ul> <li>Attended Health GIS conference and researched method for testing our ability to represent and predict where specific HLA types are most likely to be located geographically.</li> </ul>				

# Development of Medical Technology for Contingency Response to Marrow Toxic Agents April 01, 2011 through June 31, 2011

IIB 3 Task 5: Bioinformatics Web Site – This task is closed.

**IIB 3 Task 6:** Consultants to Improve Algorithm – This task is closed.

**IIB 3 Task 7:** Population Genetics – This task is closed.

**IIB 3 Task 8:** Haplotype Matching – This task is closed.

**IIB 3 Task 9:** Global Haplotype/Benchmark – This task is closed.

**IIB. Rapid Identification of Matched Donors – Objective 4:** Reducing the time and effort required to identify closely matched donors for patients in urgent need of HSC transplants will improve access to transplantation and patient survival in the context of a contingency response and routine patient care.

IIB.4 Task 1: Expand Network Communications – This task is closed.

#### IIB.4 Task 2:

#### Central Contingency Management

#### **Period 3 Activity:**

A Transplant Center (TC) study was initiated to evaluate TC search strategy proficiency in donor selection. The study includes US Transplant centers and up to five random patient searches that requested donors for search activity. Each individual search was reviewed by a Senior Strategist and was rated on three categories: patient HLA typing – loci/resolution, search strategy, and number of donors selected. These three categories were independently rated and used for a cumulative score to rate the searches. 556 searches were evaluated from 130 TCs, 76% rated in the high proficiency group and 24% in the low. The majority of searches in the low proficiency group did not select an adequate number of donors. Five factors were evaluated for correlation to proficiency: use of NMDP search services - Search Strategy Advice (SSA) or Custom Search Support (CSS), presence of Certified Hematopoietic Transplant Coordinator (CHTC) staff, URD procurements (FY 2010), and search difficulty. Univariate and Multivariate analysis found searches that received CSS, were performed at a TC with at least one CHTC on staff, and were not difficult were more likely to have a high proficiency rating.

**IIB.4 Task 3:** Benchmarking Analysis – This task is closed.

IIB.4 Task 4: Expand Capabilities of Collection and Apheresis Centers – This task is closed.

# Development of Medical Technology for Contingency Response to Marrow Toxic Agents April 01, 2011 through June 31, 2011

**IIC. Immunogenetic Studies – Objective 1:** HLA mismatches may differ in their impact on transplant outcome, therefore, it is important to identify and quantify the influence of specific HLA mismatches. In contingency situations it will not be possible to delay transplant until a perfectly matched donor can be found.

#### IIC.1 Task 1:

Donor Recipient Pair Project

#### **Period 3 Activity:**

In 1994 a retrospective D/R Pair HLA typing project to characterize class I and class II alleles of donor/recipient paired samples from NMDP's Repository was initiated. The goals of this ongoing research project are to assay the impact of DNA-based HLA matching on unrelated donor transplant outcome, develop strategies for optimal HLA matching, evaluate the impact of matching at alternative HLA loci on transplant outcome and finally to promote the development of DNA-based high resolution HLA typing methodologies. Presence/absence typing of 14 KIR loci (2DL1-5, 2DS1-5, 3DL1-3 and 3DS1) has been included.

- Auditing of 175 pairs typed for HLA and KIR in SG27 has begun. No make resolution has been and the discrepancy will be completed in the next quarter.
- Final results for SG 28 have been received, 2011 with a period of performance through July 31, 2011, 110 pairs are being typed for HLA and KIR.
- SG 29 recipient/cord pairs were selected (120) and have been contracted for typing at HLA and KIR during the period of performance of September 01, 2011 to December 31, 2011.
- To date over 2210 pairs and 1180 additional donors have been typed for presence/absence of 14 KIR loci (2DL1-5, 2DS1-5, 3DL1-3 and 3DS1).

**IIC. Immunogenetic Studies – Objective 2:** Even when patient and donor are HLA matched, GVHD occurs so other loci may play a role.

#### IIC 2 Task 1:

Analysis of non-HLA loci

#### **Period 3 Activity:**

The Immunobiology Project Results (IPR) database and its applications allow for storage and analysis of all immunogenetic data collected on NMDP research samples. This database has replaced the existing HLA donor/recipient pair's database and facilitates storage and analysis of data from other immunogenetic loci (KIR, microsatellites, single nucleotide polymorphisms, etc).

# Development of Medical Technology for Contingency Response to Marrow Toxic Agents April 01, 2011 through June 31, 2011

#### During Period 12:

- ~10 bug fixes and minor enhancements, focused on the Request Report and the Audit Tool/Report
  - o Allele codes are expanded when the mouse hovers over them.
  - o Allele searches operate on the entire database (as opposed to the screen)
- Development was completed for the migration of historical data from the legacy database into IPR.

#### Immunobiology Integration DataBase (IIDB)

• Created a schema for collection of Data Quality errors in order to flag end-users of data-quality issues and collect metrics on our cleanup processes. The work on triaging the most critical errors is in progress.

IIC 2 Task 2: Related Pairs Research Repository – This task is closed.

**IIC 2 Task 3:** CIBMTR Integration – This task is closed.

**IID.** Clinical Research in Transplantation – Objective 1: Clinical research in transplantation improves transplant outcomes and supports preparedness for a contingency response.

#### IID.1 Task 1: Observational Research, Clinical Trials and NIH Transplant Center

#### **Period 3 Activity:**

#### **Prospective Studies; RCI BMT**

- During this quarter, follow up activities continued for donors participating in the PBSC vs. Marrow clinical trial.
- Accrual on the Adult Double Cord trial was completed this quarter. Five patients were enrolled for a total of fifty-six patients. Staff continued to coordinate, manage data collection and monitor sites.
- Activities continued on the Long Term Donor Follow up project. To date, more than 9000 donors
  have been enrolled. During this period, the Survey Research Team continued to receive consents
  from the previously donated group and began to make scheduled follow up calls. Donor Centers
  are actively performing consent sessions with donors during their standard work-up process.

# Development of Medical Technology for Contingency Response to Marrow Toxic Agents April 01, 2011 through June 31, 2011

During this reporting period, database management and system updates were performed to the AdvantageEDC system being used for both the Double Cord and Revelimid trials

#### Cord Blood Research

- The analysis evaluating the likelihood of finding a non-inherited maternal antigen/allele (NIMA) match for HLA mismatched cord blood unit for transplant when upfront maternal typing is not available. The retrospective analysis compared the frequencies of the NIMA matched and mismatched HLA- A, B antigens or DRB1 alleles found in the Eurocord/NMDP/CIBMTR study to determine any significant differences.
  - o Results are being incorporated into a manuscript and will be submitted next quarter.
- Two cord blood workshops were developed for the 2011 NMDP Council Meeting.
  - New Research to Improve Cord Blood Transplant Outcomes: This workshop will offer some of the cutting-edge work focused on improving cord blood outcomes by addressing some of the limitations of the graft source.
  - o New Cord Blood Matching Concepts: This workshop will provide recent findings on extended HLA matching (role of the HLA-C locus), matching for non-inherited maternal antigens, and the impact of pre-existing cord specific anti-HLA antibodies in cord blood transplant recipients.
- The white paper detailing recommendations/guidelines for the assessment of new assays (potency or other assays) relevant to cord blood banking and/or transplantation published in Cytotherapy March 2011 has generated interest from potential industry partners.
  - Work continued on protocol development to assess interlaboratory variability utilizing the HALO assay.
  - Work continued on a study to assess CBU characteristics (viability, TNC, CFU and CD34) prefreeze and post thaw. Segment evaluation prior to unit release was under consideration as a third evaluation point. Results of a survey to the cord blood banks were analyzed and the unit

Development of Medical Technology for Contingency Response to Marrow Toxic Agents
April 01, 2011 through June 31, 2011

release testing data deemed too variable for meaningful analysis. The study will proceed with pre-freeze and post-thaw characteristics only.

#### **FormsNet Activity**

- Completed the build, quality assurance testing and implementation of the Cord Blood/ Event Reporting project. It was implemented in FormsNet to support the 10-CBA (Cord Blood Access) study and Event Reporting scope. The Event Reporting requirements included those to support reporting of Adverse Events and Product Deviations. This project was needed to support the FDA requirement to collect and display Licensure status and IND information on CBUs by October 2011. Another release will be implemented in October 2011 to support additional Adverse Event follow-up needs.
- Completed the build, quality assurance testing and implementation of the Related Donor Safety Monitoring capability into FormsNet. Related Donor Safety Monitoring is an interim approach to support monitoring of the Related Donor Safety study centers. It provides the materials required to conduct on-site monitoring visits to determine the error rate in the FormsNet database, document the error rate, identify systematic and non-systematic errors, and assess protocol compliance.
- Completed the requirements and began development of the 10-CBA Monitoring capability within FormsNet. 10-CBA Monitoring will support monitoring at centers that are enrolling subjects in the 10-CBA clinical trial. It will also provide for on-site and remote monitoring capabilities for the monitoring staff. The 10-CBA Monitoring functionality will be available for use in January 2012.
- These two interim monitoring approaches are intended for use until the full requirements for monitoring clinical trials can be completed and implemented. The full requirements to support monitoring of Clinical Trial sites and adherence to study protocols are expected to be complete in January 2012.
- Quality assurance of the mapping of the NMDP recipient legacy data (before 11/2007) to the FormsNet database continues. Several major groups of forms have completed the full migration path. NMDP Legacy data transformation to FormsNet is expected to be complete in December 2011. Definition of mapping continues for NMDP legacy data transformation from FormsNet to

# Development of Medical Technology for Contingency Response to Marrow Toxic Agents April 01, 2011 through June 31, 2011

Observational database. Full data migration planning continues.

- FormsNet 3 design planning is complete. Iterative builds and testing sprints begin in October 2011. Phase I completion targeted for October 2012.
- Quality assurance of the mapping of NMDP legacy data (before 11/2007) to the FormsNet database
- Management Reporting Website documented produced and released fifteen new reports based on FormsNet data. Requirements were for management oversight and clinical trials support.

#### **AGNIS**

- Collaborating with NCI and sharing tools developed by AGNIS team with NCI for use of non-CIBMTR curation teams
- Working with NCI to integrate current CIBMTR context for hematopoietic cell transplantation (HCT) into future data model systems, such as Biomedical Research Integrated Domain Group (BRIDG)
- Version 2.8.1, including form 2300 and defect resolution for form 2200, released 9/20/11
- Began Quality Assurance review of form 2007
- European Group for Blood and Marrow Transplantation (EBMT)/Eurocord Project: The purpose of this project is to facilitate connection of EBMT and Eurocord to AGNIS for exchange of data with European registries and cord blood banks, particularly for cord blood outcomes data
- Six forms have been completed for transfer of data from EBMT to CIBMTR
- Continued mapping form 2451 (Chimerism) from EBMT to CIBMTR
- Testing submission of form 2400 (Pre-TED)
- One site submitting forms through AGNIS; one site submitting test data; one site ready to begin testing
- Twenty sites receiving data from AGNIS (via StemSoft)
  - o One vendor (RemedyMD) has contacted AGNIS team to establish credentials and develop test

	data submission		
IID.1 Task 2: Research	h with NMDP Donors – This task is closed.		
IID.1 Task 3: Expand Immunobiology Research	Period 3 Activity:  The CIBMTR IBWC met monthly during the quarter to discuss progress on ongoing research studies  • Work continued on several draft manuscripts and analyses.  • One abstract was submitted:  • Minoo Battiwalla, et al., HLA DR15 antigen status does not impact graft-versus-host disease or disease-free survival in HLA-matched sibling transplantation for hematologic disease. Accepted for Poster presentation 2011 ASH meeting.  • Two manuscripts were published:  • Stephen Spellman et. al., Scoring HLA Class I Mismatches by HistoCheck Does Not Predict Clinical Outcome in Unrelated Hematopoietic Stem Cell Transplantation. Biology Blood Marrow Transplant. 2011 Sep 27. [Epub ahead of print] PubMed PMID:21963622.  • Mary Eapen, et al., Effect of donor-recipient HLA matching at HLA A, B, C, and DRB1 on outcomes after umbilical-cord blood transplantation for leukaemia and myelodysplastic syndrome: a retrospective analysis. Lancet Oncol. 2011 Oct 6. [Epub ahead of print] PubMed PMID: 21982422.		

#### QUARTER PROGRESS REPORT

# Development of Medical Technology for Contingency Response to Marrow Toxic Agents April 01, 2011 through June 31, 2011

#### **ACRONYM LIST**

AABB	American Association of Blood Banks	HR	High Resolution
AFA	African American	HRSA	Health Resources and Services Administration
AGNIS	A Growable Network Information System	HSC	Hematopoietic Stem Cell
AML	Acute Myelogenous Leukemia	IBWC	Immunobiology Working Committee
ABD	Antigen Binding Domain	IDM	Infectious Disease Markers
API	Asian Pacific Islander	IHWG	International Histocompatibility Working Group
ARS	Acute Radiation Syndrome (also known as Acute	IPR	Immunobiology Project Results
	Radiation Sickness)		
ASBMT	American Society for Blood and Marrow	ICRHER	International Consortium for Research on Health
	Transplantation		Effects of Radiation
ASHI	American Society for Histocompatibility and	IND	Investigational New Drug
	Immunogenetics		
B-LCLs	B-Lymphoblastoid Cell Lines	IS	Information Services
BARDA	Biomedical Advanced Research and	IT	Information Technology
	Development Authority		
BBMT	Biology of Blood and Marrow Transplant	IRB	Institutional Review Board
BCP	Business Continuity Plan	JCAHO	Joint Commission on Accreditation of Healthcare
			Organizations
BCPeX	Business Continuity Plan Exercise	KIR	Killer Immunoglobulin-like Receptor
BMCC	Bone Marrow Coordinating Center	MDACC	MD Anderson Cancer Center
BMDW	Bone Marrow Donors Worldwide	MDS	Myelodysplastic Syndrome
BMT	Bone Marrow Transplantation	MHC	Major Histocompatibility Complex
BMT CTN	Blood and Marrow Transplant - Clinical Trials	MICA	MHC Class I-Like Molecule, Chain A
	Network		
BODI	Business Objects Data Integrator	MICB	MHC Class I-Like Molecule, Chain B
BRT	Basic Radiation Training	MKE	Milwaukee
C&A	Certification and Accreditation	MRD	Minimal Residual Disease
CAU	Caucasian	MSKCC	Memorial Sloan-Kettering Cancer Center
CBMTG	Canadian Blood and Marrow Transplant Group	MSP	Minneapolis
CBB	Cord Blood Bank	MUD	Matched Unrelated Donor

#### QUARTER PROGRESS REPORT

CBC	Congressional Black Caucus	NAC	Nuclear Accident Committee
CBS	Canadian Blood Service	NCBM	National Conference of Black Mayors
CBU	Cord Blood Unit	NCI	National Cancer Institute
CHTC	Certified Hematopoeitic Transplant Coordinator	NEMO	N-locus Expectation-Maximization using
			Oligonucleotide typing data
CIBMTR	Center for International Blood & Marrow	NHLBI	National Heart Lung and Blood Institute
	Transplant Research		
CIT	CIBMTR Information Technology	NIH	National Institutes of Health
CLIA	Clinical Laboratory Improvement Amendment	NIMS	National Incident Management System
CME	Continuing Medical Education	NK	Natural Killer
CMF	Community Matching Funds	NLE	National Level Exercise
COG	Children's Oncology Group	NMDP	National Marrow Donor Program
CREG	Cross Reactive Groups	NRP	National Response Plan
CSS	Center Support Services	NST	Non-myeloablative Allogeneic Stem Cell
			Transplantation
CT	Confirmatory Testing	OCR/ICR	Optical Character Recognition/Intelligent Character
			Recognition
CTA	Clinical Trial Application	OIT	Office of Information Technology
DC	Donor Center	OMB	Office of Management and Budget
DHHS-ASPR	Department of Health and Human Service –	ONR	Office of Naval Research
	Assistant Secretary Preparedness and Response		
DIY	Do it yourself	P2P	Peer-to-Peer
DKMS	Deutsche Knochenmarkspenderdatei	PBMC	Peripheral Blood Mononuclear Cells
DMSO	Dimethylsulphoxide	PBSC	Peripheral Blood Stem Cell
DoD	Department of Defense	PCR	Polymerase Chain Reaction
DHHS-ASPR	Department of Health and Human Services –	PSA	Public Service Announcement
	Assistant Secretary for Preparedness and		
	Response		
DNA	Deoxyribonucleic Acid	QC	Quality control
DR	Disaster Recovery	RCC	Renal Cell Carcinoma
D/R	Donor/Recipient	RCI BMT	Resource for Clinical Investigations in Blood and

#### QUARTER PROGRESS REPORT

			Marrow Transplantation
EBMT	European Group for Blood and Marrow Transplantation	REAC/TS	Radiation Emergency Assistance Center/Training Site
EDC	Electronic Data Capture	RFP	Request for Proposal
EFI	European Federation of Immunogenetics	RFQ	Request for Quotation
EM	Expectation Maximization	RG	Recruitment Group
EMDIS	European Marrow Donor Information System	RITN	Radiation Injury Treatment Network
ENS	Emergency Notification System	SBT	Sequence Based Typing
ERSI	Environment Remote Sensing Institute	SCTOD	Stem Cell Therapeutics Outcome Database
FBI	Federal Bureau of Investigation	SG	Sample Group
FDA	Food and Drug Administration	SLW	STAR Link® Web
FDR	Fund Drive Request		
FLOCK	Flow Cytometry Analysis Component	SSA	Search Strategy Advice
Fst	Fixation Index	SSO	Sequence Specific Oligonucleotides
GETS	Government Emergency Telecommunications Service	SSP	Sequence Specific Primers
GCSF	Granulocyte-Colony Stimulating Factor (also known as filgrastim)	SSOP	Sequence Specific Oligonucleotide Probes
GIS	Geographic Information System	STAR®	Search, Tracking and Registry
GvHD	Graft vs Host Disease	TC	Transplant Center
HCS	HealthCare Standard	TED	Transplant Essential Data
HCT	Hematopoietic Cell Transplantation	TNC	Total Nucleated Cell
HEPP	Hospital Emergency Preparedness Program	TSA	Transportation Security Agency
HHQ	Health History Questionnaire	UI	User Interface
HHS	Health and Human Services	UML	Unified Modeling Language
HIPAA	Health Insurance Portability and Accountability	URD	Unrelated Donor
THE	Act	NIC A	Will 1 Cl. A 1'C' c'
HIS	Hispanic	WGA	Whole Genome Amplification
HLA	Human Leukocyte Antigen	WMDA	World Marrow Donor Association
HML	Histoimmunogenetics Mark-up Language	WU	Work-up